RETINOBLASTOMA IN THE ADULT

RALPH O. RYCHENER, M.D.
Memphis, Tenn.

Duke-Elder in a comprehensive discussion of primary neuro-epiblastic tumors classified them under 5 headings:

1. Retinoblastomata
2. Neuro-epitheliomata
3. Medullo-epitheliomata
4. Neurocytomata
5. Astrocytomata or true gliomata.

In general the first 2 are common, the last 3 rare. He defines retinoblastomata as malignant tumors arising in early youth, preferentially from the posterior part of the retina, composed of small, closely packed, round or polygonal cells with large, darkly staining nuclei and scanty cytoplasm. A radial arrangement around blood vessels to form pseudo-rosettes is common, degenerative changes are frequent and, as would be expected, owing to the embryonic nature of the cells, malignancy is high, usually by local extension to the brain and orbit and sometimes by distant metastases.

This classification is not accepted by America. In 1929 before this Society, Verhoeff reported the only true case of retinoblastoma in an adult recognized to that time. A review of the medical literature indicates that since that date only 6 definitely proved cases of neuro-epiblastic tumor have been recorded: a retinoblastoma in a male of 27 by O'Day, a neuro-epithelioma in a male of 67 by McCrea, and 1 in a male of 48 by Rasmussen, and astrocytomata in a male of 67 by Sempé, Dejean and Harant, in a female of 23 by McLean, and in a male of 77 by Huggert and Hultquist.

This report will then record the third case of true retinoblastoma in the adult. This was in a female of 33 whose lesion was present with good visual acuity and watched for

4½ years before retinal detachment and secondary glaucoma persuaded her to submit to enucleation.

CASE REPORT

Mrs. M. S. P., aged 33, was referred to me by Dr. Percy A. Conyers of Dyersburg, Tennessee, on February 21, 1940, because she had noted black spots before the right eye for 4 days previously. Her visual acuity with her correction of −1.00 sph. +2.50 cyl. ax. 70 was 6/7.5 and Jaeger 1. The left eye with a similar correction axis 95 had a visual acuity of 6/7.5 and Jaeger 1 and upon inspection was normal in every way. The right eye was externally normal but ophthalmoscopy disclosed numerous thready and tadpole-shaped vitreous opacities which did not cloud the fundus sufficiently to prevent recognition of an unusual cystic lesion below the optic disc, which seemed superimposed upon an old chorioretinal scar with a superior crescentic boundary of black retinal pigment. The lesion was a 3-lobed cystic affair, the upper lobe being slightly larger than the disc and about 1 D.D. below it, covered and invaded by many small vessels, giving it a pinkish appearance in contrast to the smooth-surfaced, gray, translucent appearance of the 2 much larger lobes which were joined to it below. It had somewhat the appearance of an asymmetrical 3-leaved clover. The base of the lesion could be seen through the lower lobes and seemed nonpigmented. The height of the retinal cyst was recorded as +8, the level of the optic disc and surrounding retina as +2. Peripheral lesions of old disseminated chorioretinitis were observed and this unusual fundus finding was interpreted as a cystic retinal gliosis overriding a healed lesion of chorioretinitis. Transillumination of the mass was normal except for the crescentic line of pigment marking the upper ⅔ of its boundary. Intra-ocular pressure was recorded as 13 right eye and left eye 12, Schiötz. Potassium iodide was prescribed.

One month later visual acuity was recorded as 6/6 and Jaeger 1 and the patient's symptoms were relieved. The fundus appearance was unchanged. She stated she had never previously observed any visual disturbance despite the multiplicity of chorioretinal scars, suggesting that these lesions had not been active since infancy.

She was not seen again until June 21, 1943, when she stated that some dimness of vision had come on in the past 2 months. Visual acuity was still recorded as 6/7.5 and Jaeger 1 but the visual field now disclosed a large superior temporal defect. The cystic mass had now shrunken into one pedunculated, irregular lesion, the sur-

face being rough and corrugated at an elevation of +8. The shrinking of the mass now disclosed on all sides a posterior surface of chorioretinal atrophy with pigmentation. Transillumination was as before and intra-ocular pressure was normal. She was informed that the lesion was a suspicious one and should be watched carefully.

On March 20, 1944, she returned for refraction of the left eye, stating that on December 24, 1943, the vision of the right eye was completely lost, returned slightly for a month and then again diminished to light perception. She now exhibited a complete retinal detachment with a crescentic tear up and out at 10:30 o'clock. Pigmentation of the bullous inferior lobe of the detachment was observed. Transillumination and intra-ocular pressure were still normal. In view of the probability of intra-ocular tumor, enucleation was advised but refused.

On August 23, 1944, she again returned for refraction of the left eye, stating that 5 weeks previously the right eye had pained severely enough to place her in bed for a week but was now comfortable. The chamber was shallow, the pupil quadrangular, the iris atrophic, with new-formed vessels on its surface. Vitreous opacities and complete retinal detachment were present. Transillumination of the globe still failed to cast any definite shadow but intra-ocular pressure was 50, Schiötz. The patient at this time was 37 years of age. Enucleation was performed on September 1, 1944, and the eye sent to the Army Institute of Pathology, where a preliminary diagnosis was made of malignant melanoma of the choroid, changed on final examination to retinoblastoma.

Following is the report in the case of Mrs. M. S. P., AIP Accession No. 116855:

Gross: The specimen consists of a firm eye measuring 25.5 by 25.5 by 24.5 mm. A dilated pupil is seen through the cloudy cornea. The eye is opened in the vertical plane. There are firm, gelatinous exudate and a pale growth 6.5 by 7 by 7 mm. beneath the detached retina. The tumor is situated near the optic disc. The iris and lens are displaced forward.

Microscopic: Arising in the retina adjacent to the nerve head is a tumor composed of cells with rather scanty cytoplasm and with round or nearly round nuclei of variable size. The nuclei have a rather regularly distributed chromatin network and nucleoli are either absent or ill defined. Hyperchromatic nuclei and mitotic figures are abundant and in one area there are many large bizarre and multinucleated forms. There is a marked tendency, particularly near an area of choroidal invasion, toward rosette formation.

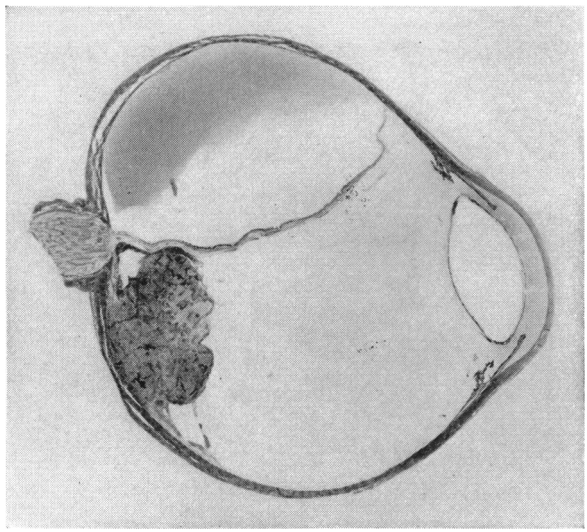

Fig. 1.—Retinoblastoma in an adult aged 38.

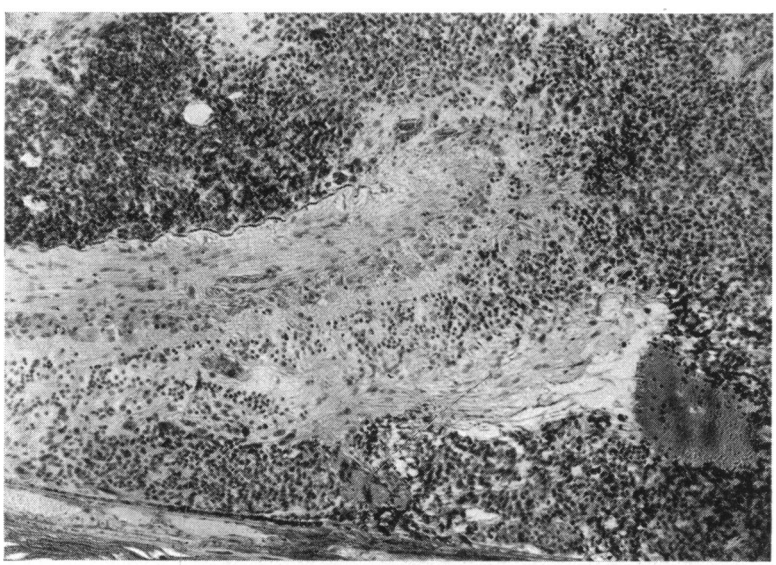

Fig. 2.—Intact membrane of Bruch in retinoblastoma in an adult.

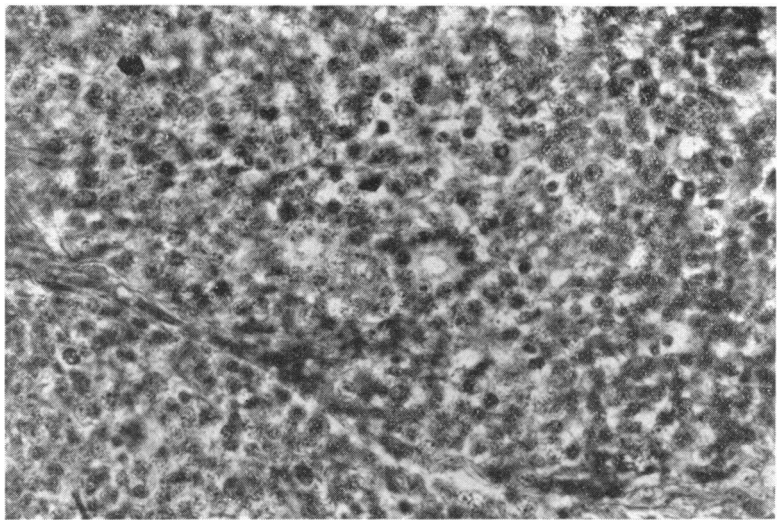

Fig. 3.—Rosette formation under low power.

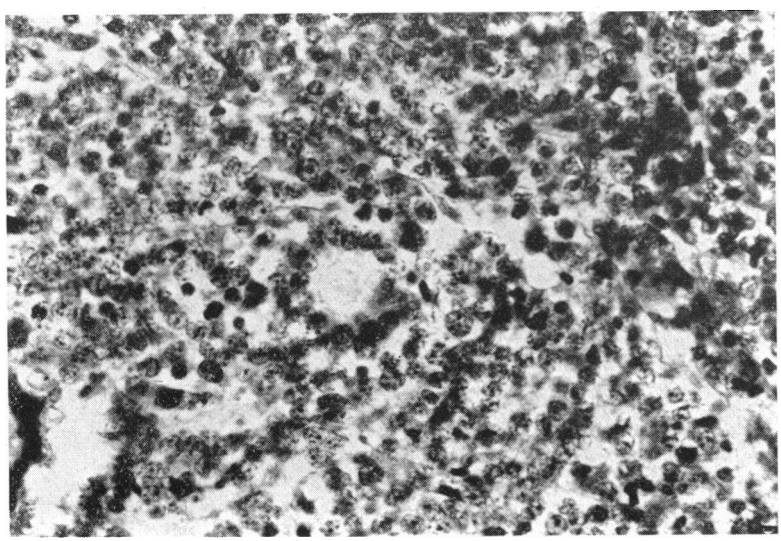

Fig. 4.—Rosette formation under high power.

Here pseudo and incomplete rosettes are seen. Only 2 or 3 true Flexner-Wintersteiner rosettes were found in over 60 sections. There is one area of necrosis and, around this, clumping of living cells about blood vessels is evident. There are blood vessels and areas of hemorrhage around the tumor. Tumor cells have seeded along the inner and outer retinal surfaces and appear in clumps both adherent to and within the retina, remote from the primary tumor. Similar clumps adhere to the inner surface of the choroid and are free in the vitreous chamber. Adjacent to the tumor the retina has undergone gliosis, fibrosis and calcification. Beneath and peripheral to the tumor there are patchy lymphocytic infiltrations of the choroid with chorioretinal adhesions, secondary pigmentation of the retina and obliterative changes in the retinal vessels.

There are broad peripheral anterior synechia, a vascular membrane on the anterior surface of the iris and ectropion uveae. The ciliary body appears somewhat atrophic and the ciliary processes are partially hyalinized. Serous exudate fills the anterior and posterior chambers and subretinal space. With hemorrhage it occupies the vitreous chamber. The retina is extensively detached. The lamina cribrosa is slightly depressed.

Diagnoses: Retinoblastoma with rosette formation in an adult; chronic chorioretinitis; detachment of retina; secondary glaucoma.

The pseudo-rosettes, the bipolar cells, areas of necrosis and contiguity to normal retinal elements make this a tumor which in a child's eye should be unhesitatingly diagnosed as a retinoblastoma (so-called glioma retinae). That it is an adult's eye is established by its size and certain changes characteristic of senile eyes but more definitely by the correlation of the fundus findings described clinically and the anatomic relationship of the tumor to the nerve head in the pathologic sections exhibited. There is no question of confusion of specimens in the laboratory.

Although the general aspects of the tumor are quite similar to those generally accepted as retinoblastoma, the rosette formations in this tumor were by no means as frequent as those in the adult retinoblastoma described by Verhoeff and the specimen required cutting in many fields to establish the diagnosis in its entirety.

Verhoeff has speculated as to the mode of origin of these tumors in adult eyes. Are they congenital in origin, arising from some congenital "anlage," or do they originate late in

life from cells which were originally normal? The presence of this tumor below the optic disc in the line of the fetal cleft suggests the possibility of a congenital anomaly in which a bit of retinal tissue was pinched off by abnormal closure of the cleft and held in a state of arrest for many years. Then, too, the chorioretinal scarring, present so conclusively on clinical ophthalmoscopy and so similar to smaller lesions of disseminated chorioretinitis in the periphery of the fundus, suggests a previous inflammatory episode, of which the patient had no knowledge, on which was superimposed a change of normal retinal elements to abnormal, malignant ones. However, similar changes have not been observed in the countless multitude of chorioretinal scars observed daily by clinicians and one is forced to the conclusion that this was a case of congenital "anlage" which for some reason was delayed in its development.

SUMMARY

This is believed to be the fifth recorded case of retinoblastoma in an adult. The tumor was observed clinically for 3½ years and studied microscopically. Pathologic section disclosed a cystic tumor below the optic nerve head, arising from the retina, showing the morphologic and staining properties of retinoblastoma.

The author wishes to acknowledge with sincere thanks the invaluable aid which Mrs. H. C. Wilder, of the Army Institute of Pathology, and Dr. Alfred Golden, of the Department of Pathology, University of Tennessee Medical School, rendered in the preparation of this report.

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DISCUSSION

DR. F. H. VERHOEFF, Boston, Mass.: My discussion is based of course upon the copy of Dr. Rychener's paper which he kindly sent me, and he has found apparently a few of these cases since then. A retinoblastoma in an adult is so unusual that, it seems to me, whoever observes such a case is in duty bound to report it. Dr. Rychener evidently agrees with me as to this and has done his duty nobly. I am gratified that he accepts my case as the first to be reported, and regret that I cannot reciprocate and accept his as the second, for actually, according to his evidence, it is the third. He has been led astray by the confusion that has arisen as to the meaning of the term retinoblastoma and hence was deceived by the fact that McCrea designated his tumor a neuro-epithelioma. I ought to know what retinoblastoma means, for I originated the term. I did this in 1924 when I was a member of a committee, of which Dr. Jackson was chairman, appointed by this Society. In 1926 the Society adopted the term, and it has since come into general use. It comprises all such malignant retinal tumors as were formerly designated gliomata or neuro-epitheliomata. As a matter of fact, in my adult case, and also in Dr. Rychener's, the tumor was just as much entitled to be called a neuro-epithelioma as was McCrea's tumor.

In the report of my case I discussed the possibility that the tumor arose from the pars plana ciliaris retinae, but the fact that both of the later tumors arose from the pars optica retinae now deprives this question of any importance.

After I had been asked to discuss this paper, I discovered that on March 3, 1945, I had received from the Registry of Pathology a section of Dr. Rychener's tumor and the following letter:

"We are sending you a slide of a tumor which we consider most unusual. Although we cannot classify it definitely as a retinoblastoma we consider it suggestive of this condition. It is, of course, not typical as was your case with Wintersteiner rosettes in a man of 48."

On March 10, 1945, I sent to the Registry the following report:

Accession No. 116855. "Retinoblastoma—so-called neuro-epithelioma type. The tumor everywhere has a tendency to form rosettes and shows many typical rosettes, some with limiting membranes and embryonic rods and cones. I have seen in children exactly similar tumors with the exception that this tumor does not show areas of necrosis of the tumor proper and has produced hyaline degeneration of the invaded retina. The tumor has grown

over the surface of the retina and has also given rise to metastatic nodules in the vitreous and on the surface of the retina. In spite of the relatively small size of the tumor, it has caused advanced secondary glaucoma with peripheral synechia, marked fibrosis of the iris and ectropion uveae. The retina is separated only on one side. The choroid has been compressed by the tumor, but has been invaded by it slightly, if at all. Judging by the small size of the tumor, the advanced glaucoma and the clinical history submitted, this tumor has been of unusually slow growth."

Since then I have received another section of the eye, and have studied both sections with reference to the clinical details now given by Dr. Rychener. In each section I find, in agreement with his ophthalmoscopic findings, an area of old healed chorioretinitis extending beneath the tumor from below, and a smaller one near the equator. At these sites the retina is not separated but is fused with the choroid. The usual cause of such lesions is, of course, hereditary or acquired syphilis. Also in accord with Dr. Rychener's clinical observations, I find just below the tumor a large retinal cyst with its inner wall ruptured.

Of the 3 cases, Dr. Rychener's was the only one in which a long duration of the tumor was definitely determined. Although the size it finally attained was considerably smaller than that of either of the other tumors, it was recognizable as a tumor at least 4½ years before removal of the eye.

Of great interest to me was the fact that Dr. Rychener found a hole in the separated retina, for I have never found a hole in a retina separated as the result of a tumor of any kind. In this case, possibly the hole was produced by the retina tearing away from the edges of an old chorioretinal adhesion.

I agree with Dr. Rychener that old chorioretinitis is not a primary cause of retinoblastoma. Nevertheless, in his particular case, it does not seem impossible that without the resulting degenerative changes, the anlage of the tumor might have forever remained dormant.

DR. GEORGIANA DVORAK-THEOBALD, Oak Park, Ill.: We are, indeed, grateful to Dr. Rychener for his presentation of another case of this tumor and for reminding us again that retinal tumors can and do occur in the adult eye. It is easy for us to accept what we have been taught and what we read in textbooks, that retinoblastoma occurs exclusively in the young eye, and we may overlook the possibility of such a tumor when we are confronted with an adult eye and consequently go astray on the clinical diagnosis.

Some 6 years ago Dr. Leona Fordon brought to the laboratory of the Illinois Eye and Ear Infirmary an eye containing a tumor of the type described by Verhoeff as a neuro-epithelioma and of much the same appearance as that of the tumor described by Verhoeff. Dr. Fordon reported the following history:

The patient, a 66-year-old woman, about 6 months previously had hit her head on a window, and shortly thereafter she noticed that she could not see to the left with her right eye. Examination revealed a large detachment of the retina in the lower temporal region of that eye. There was no pain. A reattachment operation was considered and refused. Two months later the detachment was larger and had a peculiar grayish appearance and there was a decrease in light transillumination. A diagnosis of melanoma was made and enucleation advised, but the patient refused to have the eye removed until about 4 months later when the eye had become painful. At this time the eye had no light perception, the tension was 66 mm. of mercury (Schiötz), and transillumination was negligible.

Calots showed a white tumor with a 10 mm. base on the choroid and a height of 14 mm.

Microscopic section showed a typical neuro-epithelioma, composed almost entirely of mature cells arranged in rosettes, most of which were round and many like tubules. The tumor was vascular. The first sections cut and studied showed no connection with the retina, and the base of the tumor invaded the choroid, suggesting that the growth might be metastatic. Serial section, however, showed the origin to be the outer nuclear and the rod and cone layer of the retina. The sides of the tumor were covered with a thick dense vascular connective tissue membrane, which probably encapsulated the tumor except at its origin, until its sudden expansion; this fact suggests the possibility that the tumor may have been present in a quiescent stage for some time. There were no areas of necrosis.

Duke-Elder raises the question whether such tumors originate from cell rests or are of spontaneous development. The tumor which I examined does not provide an answer to that question, but the suggested long quiescent period seems to add some weight to the cell rest origin.

The fact that 3 of the cases of retinoblastoma in the adult eye have been reported in the years since the war suggests that we are becoming increasingly aware of their presence.

DR. RALPH O. RYCHENER, closing: A member of this Society on a former occasion on the same controversial subject stated that he was not a pathologist nor the son of a pathologist, and I wish to add I am not even the grandson of one; therefore I am very grateful to my pathologist friends who have handled me so kindly.

I wish to make this point with regard to cystic lesions of the retina in detachments. Dr. Pischel has been quoted as saying that if a lesion in a detachment can be determined to be cystic it is most unlikely to be a tumor. This lesion proved to be a tumor, and on 2 other occasions in our practice we have observed cystic lesions of the retina, one of which was operated for retinal detachment, and both of which proved to be solid tumors of the choroid, so I think we must be careful in that respect, and not lay too much stress on the safety of a cystic lesion of the retina.

FAMILIAL CENTRAL AND PERIPAPILLARY CHOROIDAL SCLEROSIS ASSOCIATED WITH FAMILIAL PSEUDOXANTHOMA ELASTICUM*

BANKS ANDERSON, M.D.
Durham, N. C.

As the impact of a progressive public health program and the introduction of chemotherapeutic and antibiotic drugs progressively extends life's span, degenerative diseases become increasingly important. In 1910, less than 20% of our population was 45 years of age or older. In 1960, 33% will have passed this mark. The incidence of blindness due to degenerative and sclerosing vascular disease may be expected to parallel this shift in age percentage in the general population. Since the hereditary and familial aspects of these lesions have been relatively neglected in the voluminous literature on the subject, the family pedigree and case reports to be reported subsequently are presented in the hope that they will contribute in some small way to the understanding of at least one type of ocular vascular disease.

* From the Division of Ophthalmology, Duke University Medical School, Durham, N. C.